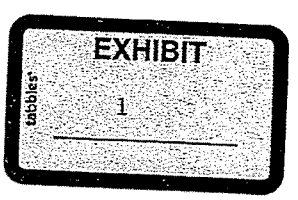
EXHIBIT 1

IN THE UNITED STATES DISTRICT COURT
DISTRICT OF DELAWARE

GLAXO GROUP LIMITED, Plaintiff, v. TEVA PHARMACEUTICALS USA, INC. AND TEVA PHARMACEUTICAL INDUSTRIES LIMITED, Defendants.	Civil Action No. 04-171-KAJ

BRADLEY D. ANDERSON, Ph.D.
FED. R. CIV. P. 26(a)(2) EXPERT WITNESS REPORT CONCERNING THE ISSUE OF INFRINGEMENT OF GLAXO'S '249 PATENT



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101. I may supplement or amend my opinions expressed in this Expert Witness Report if new or additional information is provided to me or becomes available from Teva or Teva's expert witnesses. I understand that expert reports may be provided by Teva. I reserve the right to respond to all matters raised by Teva and to testimony and opinions offered by Teva's witnesses.

Date: March 16, 2006

Bradley D. Anderson, Ph.D.

EXHIBIT 2

Ranitidine Oral Solution USP, 15mg/mL

Team Leader: Angelique Masucci

A007

Confidential
T 01994

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Confidential
T 01996

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EXHIBIT 3

Information Package: Ranitidine HCl Syrup
Revision: April 22, 2003

Redacted

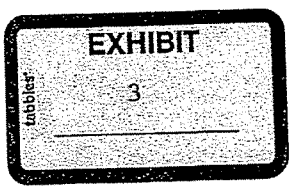

EXHIBIT 4

Confidential
T 07267

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P.D. SCALE-UP LOGBOOK

novopharm

Date Printed: Apr 08/04

EXHIBIT
7
5/19/05
PENGAD 800-631-6989

EXHIBIT
4

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EXHIBIT 5

[redacted]

novopharm

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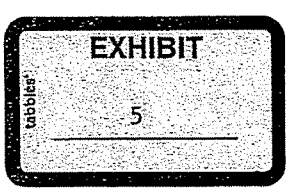

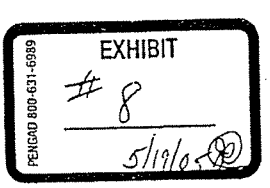

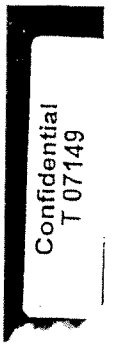

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[redacted]

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EXHIBIT 6

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

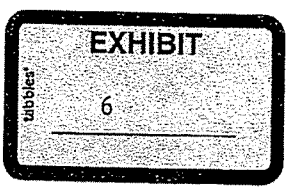
GLAXO GROUP LIMITED Plaintiff, v. TEVA PHARMACEUTICALS USA, INC. and TEVA PHARMACEUTICAL INDUSTRIES LIMITED Defendants.	Civil Action No. 04-171-KAJ

PLAINTIFF GLAXO GROUP LIMITED'S OBJECTIONS AND RESPONSES TO DEFENDANTS' FIRST SET OF REQUESTS FOR ADMISSION NOS. 1-15, 26, 27, 83-99, 101, 105 and 108-115

Pursuant to Rule 36 of the Federal Rules of Civil Procedure Plaintiff Glaxo Group Limited ("Glaxo") respond to Defendants', Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries Ltd. (collectively "Teva"), First Set of Requests For Admission Nos. 1-15, 26, 27, 83-99, 101, 105 and 108-115.

GENERAL OBJECTIONS

1. Glaxo objects to the Requests to the extent they seek information protected from disclosure by the attorney-client privilege, the work product immunity, and/or any other applicable privilege or protection. Inadvertent production of information shall not be deemed a waiver of any privilege or immunity.



Response

Denied.

Request No. 4

Admit that propylene glycol is an alcohol.

Response

Glaxo admits that in the context of the '249 patent, propylene glycol and ethanol are both organic compounds comprising a lower aliphatic hydrocarbon group with at least one -OH group, and that propylene glycol is an equivalent alcohol to the extent both are used in a stabilizing effective amount to stabilize ranitidine, otherwise denied.

Request No. 5

Admit that propylene glycol is an aliphatic alcohol.

Response

Glaxo admits that in the context of the '249 patent, propylene glycol and ethanol are both organic compounds comprising a lower aliphatic hydrocarbon group and at least one -OH group, and that propylene glycol is an equivalent alcohol to the extent both are used in a stabilizing effective amount to stabilize ranitidine, otherwise denied.

Request No. 6

Admit that propylene glycol is a lower aliphatic alcohol.

Response

Glaxo admits that in the context of the '249 patent, propylene glycol and ethanol are both organic compounds comprising a lower aliphatic hydrocarbon group with at least one -OH group, and that propylene glycol is an equivalent alcohol to the extent both are used in a stabilizing effective amount to stabilize ranitidine, otherwise denied.

4,567,178 during prosecution of the patent applications that issued as U.S. Patent No. 5,068,249 or that there was any reason to submit the patent for consideration by the U.S. Patent and Trademark Office, and therefore denies the request and leaves defendants to their proof.

Request No. 85

Admit the Teva's accused ranitidine formulation does not contain a "stabilizing effective amount of ethanol" as claimed in claims 1 through 10 of U.S. Patent No. 5,068,249.

Response

Denied.

Request No. 86

Admit the Teva's accused ranitidine formulation does not contain a "7% to 8% weight/volume ethanol based on the complete formulation" as claimed in claims 11 and 12 of U.S. Patent No. 5,068,249.

Response

Denied.

Request No. 87

Admit the Teva's accused ranitidine formulation does not literally infringe any claim of U.S. Patent No. 5,068,249.

Response

Glaxo admits that Teva's accused ANDA product, Ranitidine Oral Solution USP, 15 mg/ml does not literally contain "ethanol" as stated in the '249 patent claims, but Teva's accused ANDA product otherwise literally satisfies the claim elements in claims 1-12 of the '249 patent, and it satisfies the "ethanol" claim element by the equivalent substitution of a stabilizing effective amount of propylene glycol in place of the ethanol.

Administration ("FDA") a Notice of Claimed Investigational Exemption for a New Drug for Zantac® (ranitidine hydrochloride) Syrup" (*Glaxo v. Pharmadyne*, 32 F. Supp. 2d at 277), and that Judge Davis' statement must be put in the proper context of the entire opinion and testimony, including his finding that the use of propylene glycol in Pharmadyne's ranitidine oral solution product was the functional equivalent of ethanol in Glaxo's '249 patent, that Pharmadyne infringed the '249 patent claims and that the '249 patent claims were not invalid or unenforceable. (*Id.* at 287, 293, 303 and 313).

Request No. 90

Admit that the original formulation for Zantac® syrup included a preservative system composed of three parabens: methylparaben, propylparaben and butylparaben, but it did not contain any alcohol, and that Dr. Long noticed there was a decrease in the concentration of one of the parabens as reported in *Glaxo v. Pharmadyne*, 32 F. Supp. 2d 265 at 278.

Response

Glaxo admits only those facts to which Dr. Long testified at the trial of the *Glaxo v. Pharmadyne* action (see Trial Transcript pages 277-278 and PTX 63), which Judge Davis referred to in his opinion: "that the original formulation for Zantac® syrup included a preservative system composed of three parabens: methylparaben, propylparaben and butylparaben, but it did not contain any alcohol, and that Dr. Long noticed there was a decrease in the concentration of one of the parabens" (*Glaxo v. Pharmadyne*, 32 F. Supp. 2d at 277), and that Judge Davis' statement must be put in the proper context of the entire opinion and testimony, including his finding that the use of propylene glycol in Pharmadyne's ranitidine oral solution product was the functional equivalent of ethanol in Glaxo's '249 patent, that

Pharmadyne infringed the '249 patent claims and that the '249 patent claims were not invalid or unenforceable. (*Id.* at 287, 293, 303 and 313).

Request No. 91

Admit that Dr. Long was surprised at this decrease because there was data from a study of the formulation in sealed bottles showing there was little change in the product over a two year period as reported in *Glaxo v. Pharmadyne*, 32 F. Supp. 2d 265 at 278.

Response

Glaxo admits only those facts to which Dr. Long testified at the trial of the *Glaxo v. Pharmadyne* action (see Trial Transcript pages 280-281), which Judge Davis referred to in his opinion: "Dr. Long was surprised at this decrease because there was data from a study of the formulation in sealed bottles showing there was little change in the product over a two year period" (*Glaxo v. Pharmadyne*, 32 F. Supp. 2d at 278), and that Judge Davis' statement must be put in the proper context of the entire opinion and testimony, including his finding that the use of propylene glycol in Pharmadyne's ranitidine oral solution product was the functional equivalent of ethanol in Glaxo's '249 patent, that Pharmadyne infringed the '249 patent claims and that the '249 patent claims were not invalid or unenforceable. (*Id.* at 287, 293, 303 and 313).

Request No. 92

Admit that the degradation of the paraben concentration did not fit any known law of degradation of parabens as reported in *Glaxo v. Pharmadyne*, 32 F. Supp. 2d 265 at 278.

Response

Glaxo admits only those facts to which Dr. Long testified at the trial of the *Glaxo v. Pharmadyne* action (see Trial Transcript page 281), which Judge Davis referred to in his opinion: "the degradation of the paraben concentration did not fit any known law of degradation

of parabens" (*Glaxo v. Pharmadyne*, 32 F. Supp. 2d at 278), and that Judge Davis' statement must be put in the proper context of the entire opinion and testimony, including his finding that the use of propylene glycol in Pharmadyne's ranitidine oral solution product was the functional equivalent of ethanol in Glaxo's '249 patent, that Pharmadyne infringed the '249 patent claims and that the '249 patent claims were not invalid or unenforceable. (*Id.* at 287, 293, 303 and 313).

Request No. 93

Admit that Dr. Long had the product analyzed by Glaxo microbiologists who discovered that it contained a microbial named *pseudomonas cepacia* as reported in *Glaxo v. Pharmadyne*, 32 F. Supp. 2d 265 at 278.

Response

Glaxo admits only those facts to which Dr. Long testified at the trial of the *Glaxo v. Pharmadyne* action (see Trial Transcript pages 281-283 and PTX 239), which Judge Davis referred to in his opinion: "Dr. Long had the product analyzed by Glaxo microbiologists who discovered that it contained a microbial named *pseudomonas cepacia*" (*Glaxo v. Pharmadyne*, 32 F. Supp. 2d at 178), and that Judge Davis' statement must be put in the proper context of the entire opinion and testimony, including his finding that the use of propylene glycol in Pharmadyne's ranitidine oral solution product was the functional equivalent of ethanol in Glaxo's '249 patent, that Pharmadyne infringed the '249 patent claims and that the '249 patent claims were not invalid or unenforceable. (*Id.* at 287, 293, 303 and 313).

Request No. 94

Admit that to combat the contamination problem, Dr. Long devised a strategy that included the exploration of the use of ethanol, chlorhexidine, phenoxyethanol, benzalkonium chloride, and propylene glycol as reported in *Glaxo v. Pharmadyne*, 32 F. Supp. 2d 265 at 278.

Request No. 110

Admit that U.S. Pat. No. 4,521,431 has expired.

Response

Glaxo admits that the patent term of U.S. Patent No. 4,521,431 expired on June 4, 2002, but that Glaxo received the benefit of FDA pediatric exclusivity for Zantac® syrup until December 4, 2002.

Request No. 111

Admit the claims of U.S. Pat. No. 4,521,431 were not enforceable on or after December 9, 2003.

Response

Denied.

Request No. 112

Admit that U.S. Pat. No. 4,672,133 has expired.

Response

Glaxo admits that the term of U.S. Patent No. 4,672,133 expired on June 9, 2004.

Request No. 113

Admit the claims of U.S. Pat. No. 4,672,133 were not enforceable on or after December 9, 2003.

Response

Denied.

Request No. 114

Admit that U.S. Pat. No. 4,585,790 has expired.

Response

Glaxo admits that the patent term of U.S. Patent No. 4,585,790 expired on May 11, 2004 but that Glaxo received the benefit of FDA pediatric exclusivity for Zantac® syrup until November 11, 2004.

Request No. 115

Admit the claims of U.S. Pat. No. 4,585,790 were not enforceable on or after December 9, 2003.

Response

Denied.

Dated: March 20, 2005

CONNOLLY BOVE LODGE & HUTZ LLP

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(302) 888-6316
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New York, New York 10178-0060
(212) 309-6000

Attorneys for Plaintiff Glaxo Group Limited
453950_1

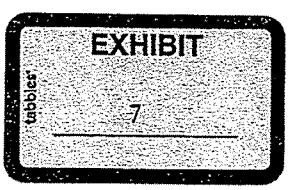
EXHIBIT 7

SECTION VI.4

BIOAVAILABILITY/BIOEQUIVALENCE: Formulation Comparison

This section contains:

- Statement of Composition of the TEVA Pharmaceuticals USA Product
- Percent Composition of the TEVA Pharmaceuticals USA Product
- Qualitative Formulation Comparison with Reference Listed Drug
- Functional Summary of Ingredients
- IIG Comparison



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RANITIDINE ORAL SOLUTION USP, 15 mg/mL
EXCIPIENT FUNCTION

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EXHIBIT 8

Trial Day 1
Volume 2 of 2
November 12, 1997

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND
NORTHERN DIVISION

GLAXO WELLCOME INC., et al. Plaintiffs v. PHARMADYNE CORPORATION, et al. Defendants	Civil Docket No. AMD-96-455 And Civil Docket No. AMD-96-1853 (Consolidated)

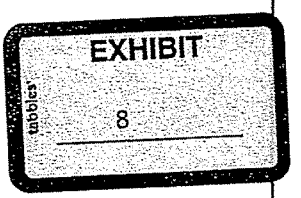
Baltimore, Maryland
November 12, 1997
2:00 p.m.

The above-entitled matter came on for trial before
The Honorable Andre M. Davis

A P P E A R A N C E S

On behalf of the Plaintiffs:
Stephen Judlowe, Esquire
John Henry Lewin, Jr., Esquire
Brian P. Murphy, Esquire
Robert Gibbons, Esquire
Regina Ambery, Esquire
Jason Lief, Esquire

On behalf of the Defendants:
James Rubin, Esquire
Alan H. Bernstein, Esquire
Robert S. Silver, Esquire
John M. Seeberger, Esquire
Deborah K. Besche, Esquire



Reported by: Betty Lou Walls, RPR

WALLS REPORTING, INC.
714 PARK AVENUE, BALTIMORE, MD 21201
410-728-9020 FAX 410-728-9024

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EXHIBIT 9

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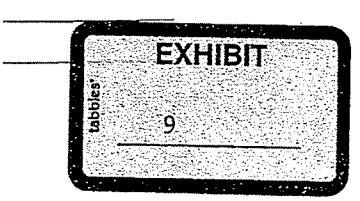

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EXHIBIT 10

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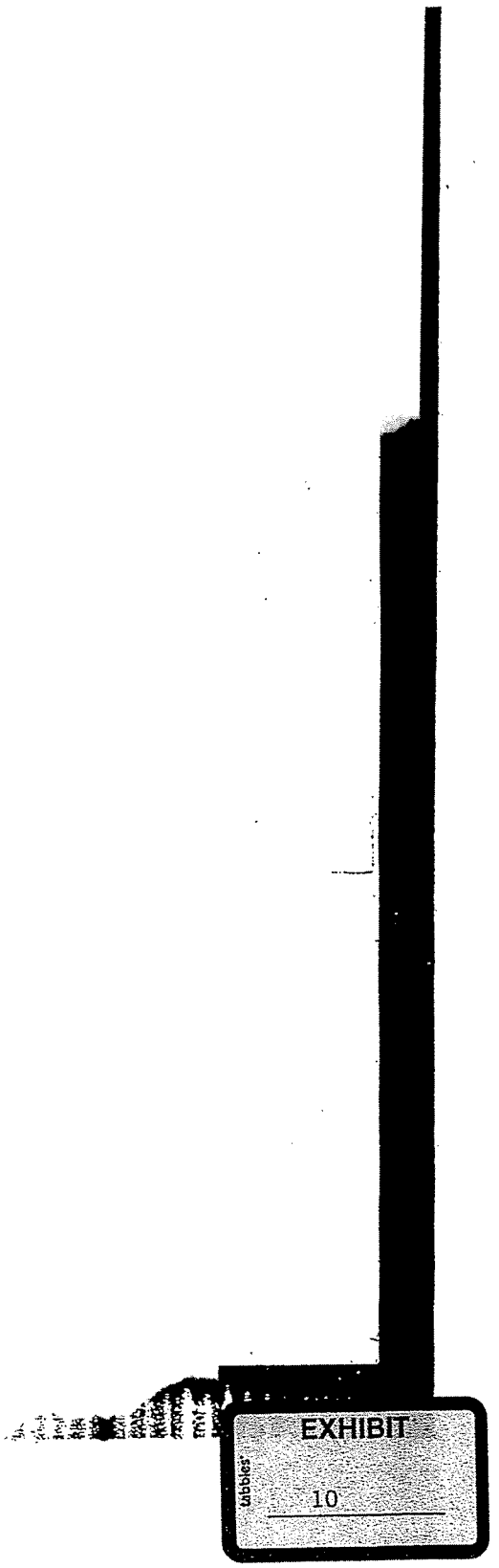

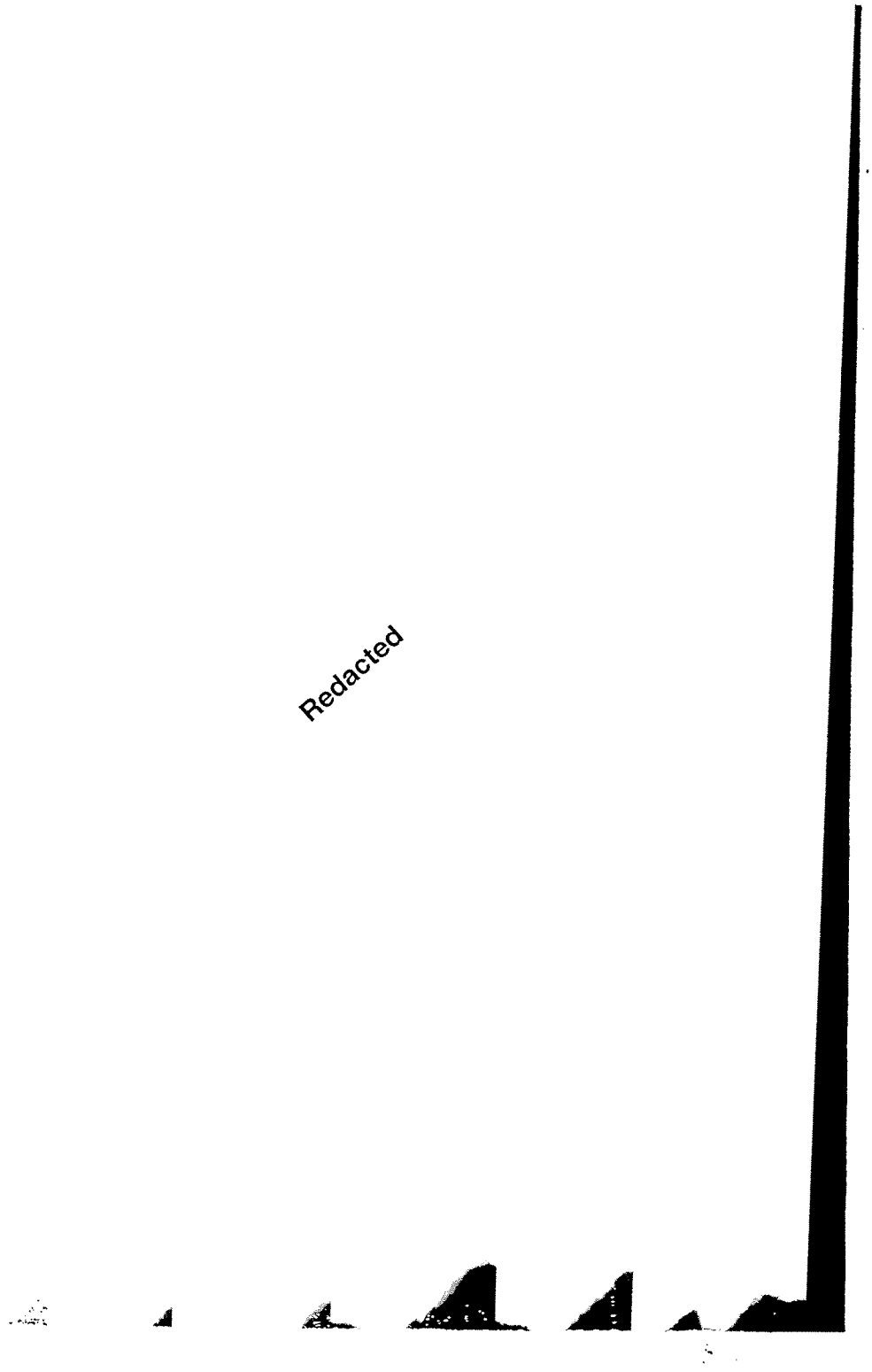
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DENTAL HEALTH

Sugar-free medicines

By M. BRANDON, BPharm, MPhil, MPS, and E. B. SADLER, BSc, MPS

THERE is irrefutable evidence that chronic administration of liquid medicines sweetened with sucrose or other fermentable sugars, such as glucose or fructose, increases the incidence of dental disease in children[1]. Many of these children may, because of their underlying illness, have serious problems with dental disease. It may, for example, lead to an increased number of dental extractions in children who present a poor anaesthetic risk[2]. It has been suggested that frequency of sugar intake is more important than the total amount ingested. Sucrose is probably the most cariogenic sugar but glucose and fructose are also highly potent. There is no evidence that the "artificial sweeteners" or sorbitol, mannitol and xylitol are cariogenic[3].

Concern has been expressed by various authorities regarding the adverse effects of the regular use of sugar-sweetened paediatric medicines and a number of pharmaceutical companies has now formulated its products with sugar-free diluents. The table below indicates those products which are sugar-free. We are grateful to the manufacturers for assistance in preparing the list and their permission for publication. If it is not possible to supply a sugar-free liquid formulation or a tablet, the pharmacist should advise the parents of children receiving "sugary" medicines to rinse the child's mouth well and to brush the child's teeth after dosing.

Table: Sugar-free medicines

ANALGESICS AND ANTI-INFLAMMATORIES		
Aspirin	Aspro Clear Claradin Disprin Junior Disprin	
Aspirin and Codeine	Anacin Codis	
Aspirin, Paracetamol and Codeine	Myalgin	
Benorylate	Benoral suspension	
Indomethacin	Indocid suspension	
Paracetamol	Panadol Soluble	
Paracetamol and Codeine	Panadeine Soluble Paracodol Solpadeine Solpadeine Forte	
Piroxicam	Feldene dispersible	
ANTACIDS		
Aluminium and Magnesium Compounds	Gelusil suspension Maalox Concentrate suspension Maalox suspension Mucogel	
Aluminium and Magnesium Compounds with Dimethicone	Andursil Antacid liquid Asilone gel Asilone Infant suspension Asilone suspension Diovol suspension Maalox Plus suspension Polycrol gel	
Aluminium and Magnesium Compounds with Alginate	Infant Gaviscon	
Hydrotalcite	Altacite Altacite Plus	
ANTICONVULSANTS		
Carbamazepine	Tegretol syrup	
Valproate	Epilim liquid	
ANTIDIARRHOEAL, ANTIEMETIC, LAXATIVES, ETC		
Hyoscyamus and Atropine	Lomotil liquid Motilium suspension	
Ispaghula	Fybogel Isogel	
Kaolin Liquid Paraffin and Phenolphthalein Loperamide Mebeverine Methylcellulose	Kaopectate Agarol Imodium syrup Colotac liquid Cologel	
Metoclopramide	Maxolon syrup Maxolon Paediatric liquid Primperan syrup	
Metoclopramide and Paracetamol	Paramax sachets	
Poloxalate and Dimethicone Sodium Picosulphate Sterculia and Frangula	Picolax Laxoberal Normacol Standard SF Formula	
ANTI-INFECTIVES		
Acyclovir	Zovirax suspension	
Amoxycillin	Amoxil dispersible tablets	
Amoxycillin and Clavulanate	Augmentin dispersible tablets Augmentin Junior suspension Augmentin Paediatric suspension	
Amphotericin	Fungilin suspension	
Ampicillin and Cloxacillin	Ampiclox Neonatal suspension	
Cotrimoxazole	Septrin dispersible tablets	
Demeclocycline	Ledermycin syrup	
Doxycycline	Vibramycin suspension	
Nalidixic	Negram suspension	
Natamycin	Pimafucin 1 per cent suspension	
Nitrofurantoin	Furadantin suspension	
Nystatin	Nystan granules for suspension	
Pivampicillin	Pondocillin suspension	
Trimethoprim	Ibral Paediatric suspension Monotrim suspension Trimopen suspension	
CARDIOVASCULAR AGENTS		
Bumetanide	Burinex liquid	
Frusemide	Lasix Paediatric liquid	
Potassium chloride	Kay-Cee-L syrup	
CNS AGENTS		
Amitriptyline	Tryptizol syrup	
Chlormethiazole	Hemineurin syrup	
Clemastine	Tavegil elixir	
Diazepam	Valium syrup	
Droperidol	Droleptan liquid	
Haloperidol	Haldol liquid 2mg/ml Haldol liquid 10mg/ml Serenace liquid	
Nortriptyline	Allertryl liquid	
Pizotifen	Sanomigran elixir	
Trazodone	Molipaxin liquid	
Trifluoperazine	Stelazine syrup	
RESPIRATORY AGENTS		
Bromhexine	Bisolvon elixir	
Brompheniramine and Decongestants	Dimotapp elixir Dimotapp elixir paediatric	
Ephedrine and Chlorpheniramine	Expurtin decongestant	
Ordiprenaline	Alupent syrup	
Ordiprenaline and Bromhexine	Alupent expectorant mixture	
Phenylpropanolamine and Diphenhydramine	Eskornade syrup	
Phenylpropanolamine and Paracetamol	Triogesic elixir	
Pholcodine	Dia-Tuss	
Pholcodine and Papaverine	Pholcomed Diabetic linctus Pholcomed Forte Diabetic linctus Pravacol-D	
Pholcodine and Phenyltoloxamine	Pholtex	
Reproterol	Bronchodil elixir	
Salbutamol	Salbulin syrup Ventolin syrup	
Terbutaline	Bricanyl syrup	
Theophylline and Ephedrine	Tedral elixir	
VITAMINS AND IRON SUPPLEMENTS		
Alfacalcidol	One-Alpha drops	
Folate	Lexpec syrup	
Iron Ederlate	Syrron	
Iron Polysaccharide Complex	Minhec elixir	
Vitamins B and C	Albee with C elixir	
Vitamins A, B and D	Ketovite (supplement) liquid	
Vitamins A, B, C and D	Vicrvel	

NB: It should be noted that some manufacturers have other liquid oral preparations with similar names to those listed, which are usually not sugar-free. The list is based on information supplied by manufacturers and the majority of sugar-free liquid preparations are included. Formulations may be altered from time to time; if in doubt, contact the manufacturer.

REFERENCES

1. *Pharmaceutical Journal*, 1981, 227, 695.
2. Roberts, I. F. and Roberts, G. J., British Medical Journal, 1979, 2, 14
3. Hobson, P., *Community Dental Health*, 1985, 2, 57

► *Mr Brandon is principal pharmacist, East Anglian Regional Drug Information Service, Ipswich hospital, and Mrs Sadler is staff pharmacist, North Western Regional Drug Information Service, St Mary's hospital, Manchester*

Society joins in campaign against sugar in medicines

THE Pharmaceutical Society has joined with the British Dental Association in writing to the Department of Health and other influential bodies to express concern about the presence of sugar in children's medicines.

A letter was sent on June 20, voicing concern about the "adverse effects of the long-term use of sugar-based medicines on the teeth of sick children". It says that at a joint meeting at the Pharmaceutical Society in 1981 the pharmaceutical industry was urged to produce a greater range of medicines containing non-cariogenic sweeteners for use by children. Although a small number of manufacturers has taken a lead and is now producing sugar-free medicines, "the majority" of children's medicines still contain sugar. The letter suggests that the use of sugar in children's medicines should be discontinued.

The letter was sent by the BDA on behalf of its dental health and science committee, the Pharmaceutical Society, the British Association for the Study of Community Dentistry, the British Paediatric Society, the British Paedodontic Society and the Health Education Council.

Two types of Nystan

SQUIBB says that it believes that many pharmacists and doctors are unaware of the availability of Nystan granules for suspension, a product which is sugar-free, and also free of lactose and corn starch.

The product is reconstituted with water to provide an oral suspension containing 100,000 units nystatin per ml. It is available in bottles of 24 doses, at a trade price of £1.67. The standard Nystan oral suspension does contain sugar.

A047

MEMORANDUM

RECEIVED
11 JUL 1985

DATE: 9 July 1985

Redacted

EXHIBIT 11

(12) UK Patent Application (19) GB (11) 2 142 820 A

(43) Application published 30 Jan 1985

(21) Application No 8412108

(22) Date of filing 11 May 1984

(30) Priority data
(31) 8313217 (32) 13 May 1983 (33) GB

(71) Applicant
Glaxo Group Limited (United Kingdom),
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(72) Inventors
John Malcolm Padfield
Ian Keith Winterborn

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High Holborn House, 52/54 High Holborn, London
WC1V 6SH

(51) INT CL⁴
A61K 31/34

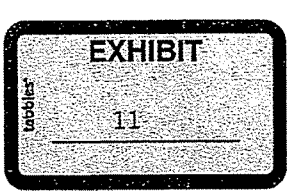
(52) Domestic classification
A5B 180 444 446 44Y 451 45Y 540 54Y 565 56Y
623 H L N
U1S 1316 A5E

(56) Documents cited
None

(58) Field of search
A5B

(54) Aqueous compositions of ranitidine

(57) Aqueous formulations of raniditine have been found to have enhanced shelf life provided that they are formulated with a pH in the range 6.5–7.5. Suitable aqueous formulations include injections for intravenous and intramuscular administration, continuous infusions and oral preparations such as syrups.



GB 2 142 820 A

073

A049

SPECIFICATION

Pharmaceutical compositions

The present invention relates to a pharmaceutical composition containing as active ingredient the histamine H_2 antagonist ranitidine.

Ranitidine [N-{2-[[5-(dimethylamino)methyl-2-furanyl]methyl]thio]ethyl}-N'-methyl-2-nitro-1,1-ethene-diamine] and its physiologically acceptable salts are described in British Patent Specification No. 1565968. In that specification there is reference to liquid formulations for oral and parenteral administrations and there is a description of an aqueous based formulation for intravenous administration and another of an oral syrup. Both of these formulations contain sufficient hydrochloric acid to achieve a pH of 5.0. In addition injection formulations are described by Padfield et al (The Chemical Use of Ranitidine, Medicine Publishing Foundation Symposium Series 5, Oxford:Medicine Publishing Formulation 1982 pp 18–22) in the form of a simple aqueous solution of ranitidine hydrochloride at its natural pH, i.e. about 5.5. Whilst such formulations containing ranitidine and/or its physiologically acceptable salts are therapeutically effective they suffer from the disadvantage of having a relatively short shelf life due to the breakdown of the ranitidine.

We have now surprisingly found that the shelf life of aqueous based formulations containing ranitidine and/or one or more of its physiologically acceptable salts may be significantly enhanced if the pH of the formulation is adjusted within the range of 6.5–7.5.

Thus the present invention provides a pharmaceutical composition which is an aqueous formulation of ranitidine and/or one or more physiologically acceptable salt thereof, having a pH within the range of 6.5–7.5. The aqueous formulation is prepared using ingredients of a purity such that it is suitable for administration to patients.

The aqueous based ranitidine formulations according to the invention are particularly stable when compared with formulations at a lower pH. Thus for example, in the case of a 25 mg/ml ranitidine hydrochloride injection solution buffered to the appropriate pH with phosphate salts and subjected to storage at 20°C, the rate of breakdown of the ranitidine is about ten times faster for a solution buffered to pH 5.5 than for a solution buffered to pH 7.0.

Conveniently the pH of the formulation according to the invention is adjusted on manufacture within the range 6.5–7.5 by means of the use of suitable buffer salts, for example, potassium dihydrogen orthophosphate and disodium hydrogen orthophosphate or citric acid and disodium hydrogen orthophosphate.

Preferred formulations according to the invention are those wherein the pH is within the range 6.7 to 7.3, for example 6.8 to 7.1.

A preferred embodiment of the invention is an aqueous formulation for parenteral administration. Such a formulation may comprise water suitable for injections in which is dissolved ranitidine and/or one or more of its physiologically acceptable salts and suitable buffer salts. Preferably the solution is adjusted to tonicity by the addition of the appropriate conventional excipients e.g. sodium chloride. Optionally the composition may also contain an antimicrobial preservative, for example phenol.

The concentration of ranitidine in formulations suitable for injection, e.g. intravenous or intramuscular injection is conveniently within the range 10–100 mg/ml, for example 25 mg/ml, expressed as free base. If desired, the solution may be diluted prior to use with, for example, an isotonic saline solution or a dextrose solution. Solutions suitable for continuous infusion may have a concentration of ranitidine of 0.1–2.0 mg/ml, preferably 0.5–1.0 mg/ml, expressed as free base. The solutions for continuous infusion may be presented in this form, for example in packs of 50–100 ml, or may be presented in a more concentrated form, i.e. 10–100 mg/ml, e.g. 25 mg/ml, for subsequent dilution before use, with, for example, an isotonic saline solution or a dextrose solution.

The aqueous formulations for parenteral administration are conveniently prepared by dissolving ranitidine and/or one or more of its physiologically acceptable salts and the excipients in water suitable for injections. The solution, which conveniently is sparged with an inert gas such as nitrogen, is sterilised preferably by filtration and then aseptically packed into suitable containers, e.g. ampoules, vials or containers for infusion, under an atmosphere of nitrogen. Alternatively the formulation may be terminally sterilized, for example by heating.

A further preferred embodiment of the invention is an aqueous formulation for oral administration. Such a formulation may comprise ranitidine and/or one or more of its physiologically acceptable salts dissolved in water, together with buffer salts, a preservative and a viscosity enhancing agent. Optionally the composition may also contain other conventional excipients such as a sweetener, a flavour and/or flavouring aids.

Suitable buffer salts for the oral formulation include potassium dihydrogen orthophosphate and disodium hydrogen orthophosphate or citric acid and disodium hydrogen orthophosphate.

Examples of suitable viscosity enhancing agents include Xanthan gum, sorbitol, glycerol,

sucrose or a cellulose derivative such as carboxymethyl cellulose or an ether thereof such as an alkyl and/or a hydroxyalkyl ether of cellulose as for example hydroxypropyl methyl-cellulose.

Suitable preservatives include the alkyl hydroxybenzoates, such as methyl, ethyl, propyl and/or butyl hydroxybenzoates.

Suitable sweeteners include saccharin sodium, sodium cyclamate, sorbitol and sucrose.

The concentration of ranitidine in the oral formulation, expressed as free base is conveniently within the range of 20–400 mg per 10 ml, for example 20–200 mg per 10 ml, more particularly 150 mg per 10 ml dose.

The aqueous formulations for oral administration are conveniently prepared by adding an aqueous solution of ranitidine and/or one or more of its salts together with the other excipients to an aqueous solution or dispersion of the viscosity enhancing agent.

The aqueous formulations according to the invention are preferably prepared using ranitidine in the form of its hydrochloride salt.

Illustrative examples of formulations according to the invention are as follows. In these examples the relative proportions of ranitidine hydrochloride and buffer salts are such that each formulation has a pH of approximately 7.

Raniditine Injection for Intravenous administration

(25 mg/ml)

Example 1

	mg/ml
Ranitidine hydrochloride	28
Potassium dihydrogen orthophosphate	0.96
Disodium hydrogen orthophosphate, anhydrous	2.4
Phenol BP	5
Water Suitable for Injections BP to	1 ml

Ranitidine hydrochloride, the buffer salts and the phenol were dissolved in Water for Injection. The solution was sparged with nitrogen, sterilised by filtration and then aseptically packed into vials under an atmosphere of nitrogen and sealed with a suitable closure.

Example 2

	mg/ml
Ranitidine hydrochloride	28
Potassium dihydrogen orthophosphate	0.96
Disodium hydrogen orthophosphate, anhydrous	2.4
Sodium chloride BP	1.6
Water Suitable for Injections BP to	1 ml

An aqueous solution of the ranitidine hydrochloride, the buffer salts and sodium chloride was prepared using Water for Injection. The solution was sparged with nitrogen, sterilised by filtration and then aseptically packed into ampoules under an atmosphere of nitrogen.

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Ranitidine oral liquid formulation (150 mg/10 ml)

Example 3

	% w/v
Ranitidine hydrochloride	1.68
Hydroxypropyl methylcellulose	q.s.
Parabens (preservative)	q.s.
Potassium dihydrogen orthophosphate	0.095
Disodium hydrogen orthophosphate, anhydrous	0.350
Sweetening agent(s)	q.s.
Flavour	q.s.
Purified Water BP to	100 ml

A solution of the ranitidine hydrochloride together with the other excipients, except hydroxypropyl methylcellulose, in purified water was added with mixing to a dispersion of the hydroxypropyl methylcellulose in purified water.

Ranitidine formulations for intravenous infusion.

	Example 4 For a 50 ml Infusion mg/ml	Example 5 For a 100 ml Infusion mg/ml
Ranitidine hydrochloride	1.12	0.56
Citric acid BP	0.3	0.3
Disodium hydrogen orthophosphate, anhydrous	1.8	1.8
Sodium chloride BP	4.5	4.5
Water Suitable for Injections BP	to 50.0 ml	to 100.0 ml

An aqueous solution of the ranitidine hydrochloride, the buffer salts and the sodium chloride is prepared using Water for Injections. The solution is sparged with nitrogen, filled into containers suitable for administering the solution by intravenous infusion, and sterilised by autoclaving.

CLAIMS

1. A pharmaceutical composition which is an aqueous formulation of ranitidine and/or one or more physiologically acceptable salts thereof, the formulation having a pH within the range 6.5–7.5.
2. A pharmaceutical composition as claimed in claim 1 having a pH in the range 6.7 to 7.3.
3. A pharmaceutical composition as claimed in claim 1 having a pH in the range 6.8 to 7.1.
4. A pharmaceutical composition as claimed in any of claims 1 to 3 in which the pH is adjusted by means of suitable buffer salts.
5. A pharmaceutical composition as claimed in claim 4 in which the buffer salts are potassium dihydrogen orthophosphate and disodium hydrogen orthophosphate or citric acid and disodium hydrogen orthophosphate.
6. A pharmaceutical composition as claimed in any of claims 1 to 5 in a form suitable for parenteral administration.
7. A pharmaceutical composition as claimed in claim 6 in a form suitable for injection and containing 10 to 100 mg/ml ranitidine, expressed as free base.
8. A pharmaceutical composition as claimed in claim 6 in a form suitable for continuous infusion and containing 0.1–2.0 mg/ml ranitidine, expressed as free base.

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9. A pharmaceutical composition as claimed in any of claims 1 to 5 in a form suitable for oral administration.

10. A pharmaceutical composition as claimed in claim 9 containing 20–400 mg per 10 ml dose.

11. A pharmaceutical composition as claimed in any of claims 1 to 10, containing ranitidine in the form of its hydrochloride salt.

12. A process for the production of a pharmaceutical composition as claimed in any of claims 1 to 11 which comprises processing the various components to provide an aqueous formulation suitable for administration to patients.

13. A process as claimed in claim 12 for the production of a composition suitable for parenteral administration, which comprises dissolving ranitidine and/or one or more physiologically acceptable salts thereof and the remaining constituents in water suitable for injection, followed by sterilisation.

14. A process as claimed in claim 12 for the production of a composition suitable for oral administration which comprises adding an aqueous solution of ranitidine and/or one or more physiologically acceptable salts thereof to an aqueous solution or dispersion of a viscosity enhancing agent.

Printed in the United Kingdom for Her Majesty's Stationery Office, Dd 8818936, 1985, 4235.
Published at The Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.

EXHIBIT 12

Subject: EFFECT OF ETHANOL ON THE STABILITY OF RANITIDINE SYRUP

Redacted

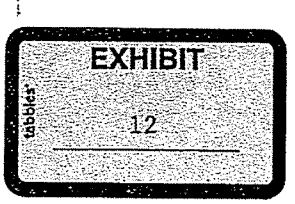

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Table 1. The effect of ethanol on the stability of Paintane Syrup (UK ingredients, glass bottles)

Redacted

Table 2 The effect of ethanol on the stability of Ranitidine Syrup (USA ingredients, glass bottles)

Redacted

Table 3. The effect of ethanol concentration* on the stability of Paricalcitol Syrup

Redacted

Table 4 The effect of citrate on the stability of Ranitidine Solutions (pH 7)

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EFFECT OF ETHANOL CONCENTRATION ON THE
STABILITY OF RANITIDINE SYRUP

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EFFECT OF ETHANOL ON THE STABILITY OF
OF RANITIDINE SYRUP (UK INGREDIENTS)

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EFFECT OF ALCOHOL ON THE STABILITY OF

RANITIDINE SYRUP (USA INGREDIENTS)

Redacted

EFFECT OF INCLUDING ETHANOL ON THE STABILITY OF RANITIDINE SOLUTIONS

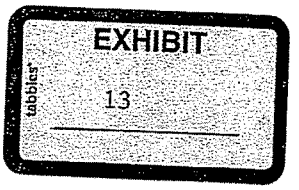
Redacted

EXHIBIT 13

IN THE UNITED STATES DISTRICT COURT
DISTRICT OF DELAWARE

GLAXO GROUP LIMITED, Plaintiff, v. TEVA PHARMACEUTICALS USA, INC. AND TEVA PHARMACEUTICAL INDUSTRIES LIMITED, Defendants.	Civil Action No. 04-171-KAJ

BRADLEY D. ANDERSON, Ph.D.
FED. R. CIV. P. 26(a)(2) REBUTTAL EXPERT WITNESS REPORT



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75. I may supplement or amend my opinions expressed in this Expert Witness Report if new or additional information is provided to me or becomes available from Teva or Teva's expert witnesses. I reserve the right to respond to all matters raised by Teva and to testimony and opinions offered by Teva's witnesses.

Date: April 24th 2006

Bradley D. Anderson, Ph.D.

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EXHIBIT 14

COPY

IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

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GLAXO GROUP LIMITED,

Plaintiff,

- against -

TEVA PHARMACEUTICALS USA, INC.,

and TEVA PHARMACEUTICAL INDUSTRIES LIMITED,

Defendants.

Civil Action No. 04-171

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101 Park Avenue
New York, New York

June 8, 2006
9:05 a.m.

Videotaped Deposition of Expert Witness, BRADLEY ANDERSON, Ph.D, taken pursuant to Agreement before Rita Persichetty, a Notary Public of the State of New York.

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EXHIBIT
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